

Appl. No.: 09/254,032
Filed: April 26, 1999
Page 2

Amendments to the Claims:

1. (Currently amended) An artificial antigen which is specifically recognized by the antifilaggrin autoantibodies present in the serum of patients suffering from rheumatoid arthritis, which consists of a recombinant or synthetic polypeptide having at least one citrulline residue, wherein said polypeptide is derived from any one of the a filaggrin variants represented by unit selected from SEQ ID NO: 7 or a fragment thereof having at least 5 consecutive amino acids residues comprising at least one arginine residue.

2. (Currently amended) The artificial antigen as claimed in claim 1, wherein said fragment of at least 5 consecutive amino acids residues of a filaggrin unit variant is selected from:

fragment 144 to 314 of SEQ ID NO: 7 or sub-fragments thereof comprising at least one arginine residue; and

fragment 76 to 144 of SEQ ID NO: 7 or sub-fragments thereof comprising at least one arginine residue.

3. (Currently amended) The artificial antigen as claimed in claim 1, wherein said fragment of at least 5 consecutive amino acids residues of a filaggrin unit variant is fragment 71-119 of SEQ ID NO: 7 or sub-fragments thereof comprising at least one arginine residue.

4. (Currently amended) The artificial antigen as claimed in claim 1, wherein said fragment of at least 5 consecutive amino acids residues of a filaggrin unit variant is selected from peptides SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 6, or sub-fragments thereof comprising at least one arginine residue.

5. (Original) Use of the antigen as claimed in any one of claims 1 to 4 for the *in vitro* diagnosis of rheumatoid arthritis.

6. (Previously amended) An antigenic composition, which contains an antigen as claimed in any one of claims 1 to 4, with the exclusion of compositions with a structure identical to that of a preparation of isoforms of filaggrin which is purified from the human epidermis

Appl. No.: 09/254,032
Filed: April 26, 1999
Page 3

comprising a mixture of isoforms having a molecular weight of 40,000 measured by SDS-PAGE and a pI ranging between 5.8 and 7.4.

7. (Withdrawn) A method of detecting the autoantibodies specific for rheumatoid arthritis in a biological sample, which method comprises:

bringing said biological sample in contact with an antigen as claimed in any one of claims 1 to 4, under conditions allowing the formation of an antigen/antibody complex with the autoantibodies specific for rheumatoid arthritis which may be present;

detecting the antigen/antibody complex which may be formed.

E, 8. (Withdrawn) A kit for the detection of autoantibodies specific for rheumatoid arthritis in a biological sample, which comprises at least one antigen as claimed in any one of claims 1 to 4, as well as buffers and reagents appropriate for constituting a reaction medium allowing the formation of an antigen/antibody complex.

9. (Withdrawn) A method of detecting the autoantibodies specific for rheumatoid arthritis in a biological sample, which method comprises:

bringing said biological sample into contact with an antigenic composition as claimed in claim 6, under conditions allowing the formation of an antigen/antibody complex with the autoantibodies specific for rheumatoid arthritis which may be present;

detecting the antigen/antibody complex which may be formed.

10. (Withdrawn) A kit for the detection of autoantibodies specific for rheumatoid arthritis in a biological sample, which comprises at least one antigenic composition as claimed in claim 6, as well as buffers and reagents appropriate for constituting a reaction medium allowing the formation of an antigen/antibody complex.

11. (Withdrawn) The composition of claim 6 wherein the antigen is labeled.

12. (Withdrawn) The composition of claim 6 wherein the antigen is conjugated with a carrier molecule.

Appl. No.: 09/254,032

Filed: April 26, 1999

Page 4

13. (Withdrawn) A process for preparing an artificial antigen which is specifically recognized by the antifilaggrin autoantibodies present in the serum of patients suffering from rheumatoid arthritis, wherein said process comprises:

providing a recombinant or synthetic polypeptide consisting of a flaggrin unit of SEQ ID NO: 7 or a fragment thereof of at least 5 consecutive amino acids comprising at least one arginine residue;

replacing at least one arginine residue of said polypeptide with a citrulline residue; and recovering the citrullinated peptide recognized by the serum of patients suffering from rheumatoid arthritis.

E, 14. (Withdrawn) A process of claim 13, wherein the replacement of arginine with citrulline is made by deimination of said arginine by a peptidylarginine deiminase.

15. (Withdrawn) A process of claim 13, wherein the replacement of arginine with citrulline is made by incorporation of one or more citrulline residues in place of one or more arginine residues during synthesis of the peptide.

16. (Withdrawn) A process for preparing an antigenic composition wherein said process comprises:

preparing an artificial antigen by the process of claim 13; and incorporating said antigen into a composition.

17. (Withdrawn) A process of claim 16 further comprising labeling said artificial antigen.

18. (Withdrawn) A process of claim 16 further comprising conjugating said antigen with a carrier molecule.

19. (Withdrawn) A method for the *in vitro* diagnosis of rheumatoid arthritis comprising the steps of:

preparing an artificial antigen by the process of claim 13;

Appl. No.: 09/254,032

Filed: April 26, 1999

Page 5

providing a biological sample for diagnosis of rheumatoid arthritis;

bringing said biological sample into contact with said artificial antigen under conditions

E, allowing the formation of an antigen/antibody complex with the autoantibodies specific for rheumatoid arthritis which may be present in said biological sample; and

detecting, by any appropriate means, the antigen/antibody complex which may be formed.
